II. Amendments

Claims 33-35, 38, 42-44, 50-53, 59 and 61-63 have been amended. The amended claims contain no new matter and are fully supported by the specification. The claims have been amended to more particularly point out what the applicant considers as his invention. The applicant contends that all pending claims as currently drafted and now amended are allowable.

III. Rejections under 35 U.S.C. 112(2)

Claim 50 has been rejected under 35 U.S.C. 112, second paragraph for being indefinite for depending upon canceled claims. Applicant addresses this rejection through amendment. Claim 50 is now dependent upon allowed claim 47 and thus is allowable through its dependency.

IV. Rejections under 35 U.S.C. 102

Claims 33-34, 38, 51-53, and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Weuffen (USP 5,629,002). Claims 33-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Hechtman (USP 5,595,753). The applicant respectfully disagrees and responds through both argument and amendment.

In Motorola, Inc. v. Interdigital Tech. Corp., 121 F.3d 1461, 43 USPQ 2d 1481, 1490 (Fed. Cir. 1997) the court states that: *"For a prior art reference to anticipate a claim, the reference must disclose each and every element of the claim with sufficient clarity to prove its existence in the prior art . . .Although this disclosure requirement presupposes the knowledge of one skilled in the art of the claimed invention, that*

presumed knowledge does not grant a license to read into the prior art reference teachings that are not there." The applicant states that the originally drafted claims were not anticipated by the Weuffen '002 disclosure. The applicant amends claims 33-34, 38, 51-53 and 59 through the removal of L-arginine, and specificly claiming L-arginine derivatives not disclosed in the Weuffen '002 patent.

Therefore the Weuffen '002 patent does not disclose each and every element of the instant application's rejected claims. The applicant respectfully requests that the rejection of claims 33-34, 38, 51-53, and 59 in view of Weuffen be removed and the claims be allowed.

The Hechtman '753 patent discloses L-arginine and N^G-nitro-L-arginine methyl ester mixed with K-Y jelly or an electrolyte solution to treat spasming sphincters. The instant invention's claims have been amended and the instant invention now does not claim L-arginine only the specific derivatives. Therefore because the Hechtman '753 patent does not contain each and every limitation of the rejected claims of the instant application the rejection should be removed and the claims allowed.

V. Rejection Under 35 U.S.C. 103(a)

Claims 33-34, 38, 51-53, and 59 are rejected under 35 U.S.C. 103(a) as being anticipated by Weuffen (USP 5,629,002). Claims 33-34 are rejected under 35 U.S.C. 103(a) as being anticipated by Hechtman (USP 5,595,753). The applicant respectfully disagrees and responds through both argument and amendment.

The Federal Circuit held that "[t]he test for obviousness is not whether the features of one reference may be bodily incorporated into another reference. . . .

Rather, we look to see whether combined teachings render the claimed subject matter obvious." See In re Wood, 599 F.2d 1032, 202 USPQ 171, 174 (C.C.P.A. 1979)(emphasis added) (citing In re Bozek, 416 F.2d 1385, 1390, 163 USPQ 545, 549-50 (C.C.P.A. 1969))

The Weuffen '002 patent specifically teaches in Example 6 and 7 in column 13, lines 19-22 that the *"importance. . . of the blood circulation in the scalp for the health of the hair, the effectively of the $SCN^{(-)}$ application was examined using a commercially available locally active vasodilator"* The specific solution is taught through the use of propyl nicotinate as displayed in Example 7 specifically in column 13, lines 44-49; *"A convincing stimulation of the growth of the hair was determinable upon the application of the combination of sodium thiocyanate and propyl nicotinate which was superior by 0.7 points according to table 1, to that of the use of the thiocyanate alone."* The Weuffen '002 patent teaches a specific method for increasing hair growth through the use of increased blood flow diametrically opposed to the method used in the instant invention.

The office cites Weuffen's Example 10 to provide the motivation for the use of L-arginine to grow hair. Contrary to the Office's assertion the Weuffen disclosure specifically teaches the use of sodium thiocyanate in combination with an amino acid solution that contains L-arginine along with all other amino acids. The disclosure provides no guidance for one to topically apply L-arginine solely as the active ingredient. The Weuffen disclosure then specifically teaches in column 14, lines 64-67 that; *"Moreover, there is a possibly provided an improved bioavailability of thiocyanate by the addition of short-chain and higher molecular weight peptides and/or proteins."*

Therefore the disclosure teaches the improved performance of thiocyanate with the addition of a peptide protein blend and not the instant claimed invention. The Office uses improper hindsight to reject the claims based upon the applicant's own disclosure.

The applicant has amended claims to incorporate specific L-arginine derivatives that are not disclosed in the prior art and it is not directed to a nitric oxide releasing substance but to a substance containing specific derivatives. Furthermore L-arginine is not a nitric oxide releasing substance but is formed as a byproduct through biological processes. Therefore the Office should remove the obviousness rejection because the art cited fails to teach each and every element of the instant claims.

The Office rejects claims 33-34 as obvious in view of the Hechtman '753 patent. The applicant respectfully disagrees with the Office and responds through both argument and amendment. Claims 33-34 have been amended to clarify and more specifically point out the applicant's invention through the specific claiming of L-arginine derivatives not disclosed in the Hechtman '753 disclosure. Claims 33-34 have now been amended to be clearly directed to increasing the bloodflow to localized tissues to aid in sexual function and assist in the repair of wounds and hair growth.

Therefore the amended claims 33-34 are allowable as amended because Hechtman does not teach or disclose either singly or in combination the specifically claimed L-arginine derivatives, nor their intended uses. The method is clearly directed to a different use than the Hechtman '753 patent which is directed to the reduction of sphincter spasms and hemorrhoidal pain. The applicant claims a different compound for a method of treating different ailments. Therefore the applicant respectfully requests

that the Office remove the obviousness rejection in light of the arguments and amendments provided.

Claims 33-35, 38, 42-44, 50-53, 59 and 61-63 are rejected under 35 U.S.C. 103(a) over Garfield et al. in view of Hechtman, Altadonna (USP 5,853,768), Cooke et al. (USP 5,428,070), Saavedra et al. (USP 5,632,981) and Cooper et al. The applicant responds through argument and amendment.

The Office cites Garfield '738 as disclosing the process of healing wounds, treating impotence and restoring hair growth by topical application of a nitric oxide donor. The abstract of Garfield '738 patent teaches the use of *"nitric oxide donors of the instant invention have a NONOate anion linked to an ortho-substituted aryl, a heteroaromatic substituent, asteroid, or a catecholamine"* as their specific nitric oxide donors and not the instant invention's specifically claimed L-arginine derivatives. The Garfield '738 disclosure teaches away from the use of L-arginine in its background as a treatment for the above mentioned disorders when in the background it states that "*Stimulated macrophages produce nitric oxide from L-arginine and it is considered the first line of defense against invading pathogens*" and then it continues with a list of present NO donor compounds in Table 1 in which L-arginine is absent.

Garfield specifically teaches that L-arginine is metabolized by the body for cellular defense but it is not recognized for treatment of any treatments accorded by the Office. Therefore it is improper to cite the Garfield '738 patent against the instant invention either singly or in combination because it teaches away from the instant invention. Furthermore the claim has been amended to remove the NO donor reference and it is limited to specifically named L-arginine derivatives. Thus without improper use

of hindsight from the applicants disclosure the cited reference fails to teach the instant invention and provides contrary motivation because with knowledge of its properties it is not considered an effective NO donor. Thus the Garfield '738 patent clearly teaches away from the instant inventions claimed method of treating aliments.

The Office cites in combination Hechtman '753 patent and states that it discloses that arginine may be applied topically to enhance nitric oxide production in tissues. However as discussed above Hechtman '753 discloses that L-arginine is useful for the treating of spasming smooth muscles, specifically sphincters. The Hechtman '753 patent provides no motivation to use L-arginine for the treatment of the disorders cited in Garfield. Furthermore the combination of Hechtman and Garfield would be incorrect because it is improper to combine a reference which teaches away with one that is silent to provide the alleged motivation to produce the instant invention without resorting to improper hindsight.

The Office cites Cooke '070 patent for it alleged teaching of that arginine glutamate functions to release nitric oxide in tissues. The Office is incorrect because it teaches in column 4, lines 63-66 teaches that "*Instead of oral administration, intravascular administration may also be employed, particularly where more rapid enhancement of the nitric oxide level in the vascular system is desired*". The internal ingestion of L-arginine to increase the nitric oxide level does not teach the topical administration of L-arginine to the skin. The Cooke '070 patent provides no teaching with reference to the instant invention because it teaches of the internal use of a known amino acid which provides no guidance without the use of the applicant's own teachings. The Cooke '070 patent fails to teach the application of L-arginine to the skin

topically to treat tissues and does not provide any suggestion that the topical application of L-arginine would have any benefit. Therefore the Office should remove the obvious rejection in light of the fact that the Cooke '070 patent fails to provide adequate motivation for the external use of L-arginine.

The Office cites Altodonna '768 for the iodide salts to increase penetration of topically applied medicaments. The Altodonna '768 patent discloses sodium iodide whereas the instant application is limited to specifically selected salts that do not include sodium iodide and therefore it is effectively removed as a reference because it fails to disclose the instant invention either singly or in combination.

The Office cites Saavedra '981 for the disclosure of treating impotence by placing a nitric oxide generating substance inside a condom and then placing the condom on the penis. The Saavedra '981 disclosure discusses the ability of the body to metabolize L-arginine internally to produce nitric oxide. However the Saavedra '981 disclosure does not teach the topical use of L-arginine nor the use of L-arginine to treat impotence. The Office incorrectly uses the teaching of the applicant's own invention to provide the motivation to combine the references.

MARKED-UP CLAIMS

33. (Twice Amended) A method of increasing localized bloodflow in tissues to increase growth rate and repair of cells by delivering a [nitric oxide releasing] substance selected from the group consisting of L-arginine hydrochloride, L-arginine glutamate, L-arginine butyrate, L-arginine glycolate, L-arginine ethyl , L-arginine methyl, L-arginine propyl, L-

arginine butyl, L-arginine isobutyl, [salts and] L-arginine t-butyl, L-arginine ethyl ester, L-arginine propyl ester, L-arginine isopropyl ester, L-arginine butyl ester, L-arginine isobutyl ester, L-arginine t-butyl ester, and mixtures thereof [derivatives], to skin comprising the step of topically applying to the skin a delivery vehicle for the substance, said delivery vehicle containing an effective amount of the substance, and a concentration of an ionic salt sufficient to create a hostile biophysical environment wherein the ionic salt is selected from the group consisting of sodium chloride, choline chloride, potassium chloride, lithium chloride and magnesium chloride and mixtures thereof which causes the substance to migrate from the delivery vehicle to the skin where the substance is absorbed by tissue.

34. (Twice Amended) The method of claim 33 wherein the delivery vehicle selected from the group consisting of topical creams, topical liquids, topical lotions and topical ointments containing the substance and the ionic salt wherein the ionic salt is a mixture consisting of sodium chloride (0.25% to 25%), choline chloride(0.25% to 25%), and magnesium chloride (0.25% to 25%) is applied to the skin.

35. (Amended) The method of claim 33 wherein a hydrophobic delivery vehicle containing the substance and the ionic salt, wherein the ionic salt is a mixture consisting of sodium chloride (0.25% to 25%), choline chloride(0.25% to 25%), and magnesium chloride (0.25% to 25%) by weight of the hydrophobic delivery vehicle is applied to the skin.

38. (Amended) The method of claim 33 wherein a transdermal patch containing the delivery vehicle and a penetrating agent is applied to the skin.

42. (Twice Amended) A method of treating impotence in a male comprising delivering a [nitric oxide releasing] substance selected from[a member of] the group consisting of L-arginine hydrochloride ,L-arginine glutamate, L-arginine butyrate, L-arginine glycolate, L-arginine ethyl , L-arginine methyl, L-arginine propyl, L-arginine butyl, L-arginine isobutyl, [salts] and L-arginine t-butyl, L-arginine ethyl ester, L-arginine propyl ester, L-arginine isopropyl ester, L-arginine butyl ester, L-arginine isobutyl ester, L-arginine t-butyl ester, and mixtures thereof [derivatives,] to the penis by topically applying to the penis a delivery vehicle for the substance, said delivery vehicle containing an effective amount of the substance, and a concentration of ionic salt selected from the group consisting of sodium chloride, choline chloride potassium chloride, lithium chloride and magnesium chloride and mixtures thereof sufficient to create [an] a hostile biophysical environment which causes the substance to migrate from the vehicle to the penis where the substance is absorbed by tissue.

43. (Twice Amended) The method of claim 42 wherein the delivery vehicle selected from a member of the group consisting of topical creams, topical liquids, topical lotions and topical ointments containing the substance wherein the substance is L-arginine hydrochloride .25% to 25% by weight and the ionic salt is choline chloride at 10% by weight, sodium chloride at 10% by weight and magnesium chloride at 5% by weight.

44. (Amended) The method of claim 42 wherein a hydrophobic delivery vehicle containing the substance wherein the substance is L-arginine hydrochloride at 12.5% by weight and the ionic salt is choline chloride at 10% by weight, sodium chloride at 10% by weight and magnesium chloride at 5% by weight is applied to the penis.

50. (Amended) The method according to [any of the preceding claims] claim 47 wherein the delivery vehicle is contained in a condom which is placed on the penis.

51. (Twice Amended) A method of promoting hair growth comprising delivering a [nitric oxide releasing] substance selected from a member of the group consisting of L-arginine hydrochloride, L-arginine glutamate, L-arginine butyrate, L-arginine glycolate, L-arginine ethyl , L-arginine methyl, L-arginine propyl, L-arginine butyl, L-arginine isobutyl, [salts] and L-arginine t-butyl, L-arginine ethyl ester, L-arginine propyl ester, L-arginine isopropyl ester, L-arginine butyl ester, L-arginine isobutyl ester, L-arginine t-butyl ester, and mixtures thereof [derivatives], wherein a selected area of the skin where hair growth is desired by topically applying to the selected area of skin where hair growth is desired a delivery vehicle for the substance, said delivery vehicle containing an effective amount of the substance, and a concentration of ionic salt selected from the group consisting of sodium chloride, choline chloride, potassium chloride, lithium chloride and magnesium chloride and mixtures thereof sufficient to create [an] a hostile biophysical environment which causes the substance to migrate from the vehicle to the selected area of skin where the substance is absorbed by tissue.

52. (Twice Amended) The method of claim 51 wherein the delivery vehicle is selected from [a member of] the group consisting of topical creams, topical liquids, topical lotions and topical ointments and is applied to the selected area of skin where hair growth is desired wherein the ionic salt is a mixture consisting of sodium chloride (0.25% to 25%), choline chloride(0.25% to 25%), and magnesium chloride (0.25% to 25%) and mixtures thereof.

53. (Amended) The method of claim 51 wherein a hydrophobic delivery vehicle containing the substance, a penetrating agent, and the ionic salt is applied to the selected area of skin where hair growth is desired.

59. (Twice Amended) The method of claim 51 wherein a transdermal patch containing the delivery vehicle, wherein the substance in the delivery vehicle is selected from a group consisting of L-arginine glutamate (0.25% to 25%), L-arginine hydrochloride (0.25% to 25%) and mixtures thereof is applied to the skin where hair growth is desired.

61. (Amended) A method of delivering a [nitric oxide releasing] substance selected from [a member of] the group consisting of L-arginine hydrochloride, L-arginine glutamate, L-arginine butyrate, L-arginine glycolate, L-arginine ethyl , L-arginine methyl, L-arginine propyl, L-arginine butyl, L-arginine isobutyl, [salts] and L-arginine t-butyl, L-arginine ethyl ester, L-arginine propyl ester, L-arginine isopropyl ester, L-arginine butyl ester, L-arginine isobutyl ester, L-arginine t-butyl ester, and mixtures thereof [derivatives], to skin comprising the step of topically applying to the skin a delivery vehicle for the substance, said delivery vehicle containing an effective amount of the

substance within a packaging selected from the group consisting of a liposome, emulsion of collagen, or collagen peptides said [liposome] packaging being at a concentration sufficient to create an hostile biophysical environment which causes the liposome to migrate from the delivery vehicle to the skin where the substance is released from the [liposome] packaging and absorbed by tissue.

62. (Amended) The method of claim 61 wherein the delivery vehicle for the substance is applied to the penis so that the [liposomes] packaging migrate from the delivery vehicle to the penis where the substance is released from the [liposome] packaging and absorbed by tissue.

63. (Amended) The method of claim 61 wherein the delivery vehicle for the substance is applied to the selected area of skin where hair growth is desired so that the [liposomes] packaging migrate from the delivery vehicle to the skin where the substance is released from the [liposome] packaging and absorbed by tissue.

III. Conclusion

The above arguments and amendments address all issues cited in the prior art. The above cited references fails to produce the instant invention either singly or in combination. For the foregoing reasons, Applicants believe this application is in condition for allowance, which is respectfully requested.

Respectfully submitted,

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